REMARKS

The Rejection Under 35 USC § 112, first paragraph

This rejection is moot in view of the cancellation of the prodrugs from the claims. The cancellation is made without prejudice or disclaimer.

The Rejection Under 35 USC § 112, second paragraph

The forms of the claims are corrected, rendering moot this rejection.

Obviousness-type Double Patenting Rejection

US 10/541,493 has been abandoned. Thus, this rejection is moot.

The Rejections Under 35 USC § 103

The claims are rejected as allegedly obvious over US 6,323,240 in view of US 6,572,542.

The claims of the present application recite specific 2-... **thio**-...-oxobutanoic group containing compounds. That is, a S group is attached in position 2 of the claimed compounds with further groups attached to said S group. Neither reference teaches or suggests any compound with a thiol group, and definitely not any of the specific compounds recited in the claims.

US '240 in its broadest disclosure recites thiol as one of the many options for any of R_1 through R_4. However, not a single compound with a thiol group is taught in the disclosure of the reference. Moreover, not a single thiol group even apart from an overall structure is identified in US '240. Merely, a broad recitation of "thiol" is made in the disclosure of US '240.

The definition of thiol is "a sulfur-containing organic compound having the general formula RSH, where R is another element or radical ... Also called mercaptan." (Emphasis added.) See The American Heritage® Science Dictionary, Copyright © 2002 by Houghton Mifflin Company, Published by Houghton Mifflin Company. Mercaptan is defined as a "sulfur-containing organic compound with the general formula RSH where R is any radical, especially ethyl mercaptan, C_2H_5SH. Also called thiol." (Emphasis added.) See The American Heritage® Dictionary of the English Language, Fourth Edition, Copyright © 2006 by Houghton Mifflin Company, Published by Houghton Mifflin Company.

Thus, one of ordinary skill in the art would understand the disclosure of US '240 as

reciting a group with any R group attached to the S group. However, a broad recitation of "any" group in a given position is not adequate to render obvious the specific compounds of the present claims. For example, in claim 16, the first named compound has a benzyl group attached to the S group, the second named compound has a methylphenyl group attached to the S group, etc. No such groups are described in US '240 with any specificity. One of ordinary skill in the art would thus not have found a reason to select, e.g., benzyl or methylphenyl, etc., groups attached to the S group.

In sum, the prior art general formula at issue here generically encompasses an extremely large number of individual compounds, especially so in view of any group being possible as the R group in a thiol group, in case a thiol group would have been selected from the generic disclosure for position 2, for which selection there is also no reason provided in US '240.

In a situation like this, the non-obviousness of the claimed compounds is controlled by strong Federal Circuit precedent. Exemplary such Federal Circuit cases include *In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992) and *In re Baird*, 16 F.2d 380, 29 U.S.P.Q. 2d 1550 (Fed. Cir. 1994).

In both *Jones* and *Baird*, the general disclosures of the references encompassed a very large number of individual compounds.

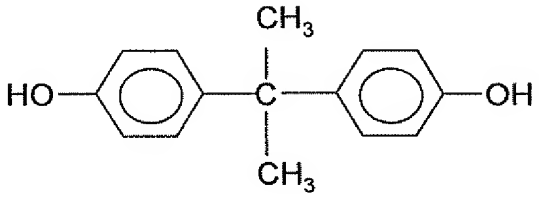
In *Jones* the Federal Circuit held that:

> We decline to extract from *Merck* the rule that the Solicitor appears to suggest – that regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it. ... In contrast, though Richter discloses the potentially infinite genus of "substituted ammonium salts" of dicamba, and lists several such salts, the salt claimed here is not specifically disclosed. Nor, as we have explained above, is the claimed salt sufficiently similar in structure to those specifically disclosed in Richter as to render it *prima facie* obvious. (21 U.S.P.Q. 2d at 1943)

While the claimed compounds may fall within the scope of US '240, there is no reason for one of ordinary skill in the art to select any of them from among the very large number of compounds generically encompassed. There is no specific disclosure in US '240 which would lead one of ordinary skill in the art to prepare any of the claimed compounds; for example, nothing provides a reason to a skilled worker to make a compound, e.g., with a benzylthio group, or a methylphenylthio group, ..., naphthylthio group, etc. Without any

reason provided for the preparation of such compounds, there cannot be a prima facie case of obviousness in view of *Jones* and many other decisions on this issue.

The lack of obviousness in the present case is even stronger than in, e.g., *Baird*. *Baird*'s claimed compounds had the following structure:



wherein each of the two OH-groups was esterified with one of three dicarboxylic acids (succinic (4 carbon atoms), glutaric (5 carbon atoms) or adipic (6 carbon atoms).) The reference had a very broad general formula encompassing, in very general terms, compounds possessing both components of Baird's claims, i.e., the above-pictured central diphenyl moiety (bisphenol A) and the terminal dicarboxylic acid esterifying groups. However, the general formula also disclosed the possibility of highly varied substitution on each of the phenyl rings, the possibility that the central three carbon atom propyl moiety to which each phenyl group is joined in the bisphenol A structure pictured above could instead also be a very wide variety of groups such as other alkylene groups, alkylidene groups or cycloalkylidene groups. Instead of the hydroxy groups at the terminal positions of bisphenol A, the phenyl rings in the reference could also be any of a large variety of possibilities, where between the O atom and the H atom of hydroxyl, there could be present $(RO)_x$ groups which were the same or different. The reference also specifically named, among twenty typical dicarboxylic acids for esterification, the three recited in Baird's claim.

The Court in *Baird* relied on the *Jones* holding quoted above, to quickly dismiss the Patent and Trademark Office's contention that the generally encompassing formula alone was sufficient to render Baird's claimed species obvious. The Court concluded that given (a) the vast number of diphenols encompassed by the reference's general disclosure, and (b) that the mentioned diphenols more specifically disclosed by the reference as typical, preferred or optimum were different from *Baird's* bisphenol A structure, the reference did not suggest the selection of bisphenol A.

Here, not even a specific disclosure as in Baird is present. All the compounds identified in US '240 are compounds which do not contain a thiol group in any position.

Moreover, in US '240 alkylthio is also an option for R_1 through R_4, and a specific compound with either R_1 or R_3 being thiomethyl is prepared (see column 5, line 47). However, alkylthio groups are irrelevant to rendering any thiol group obvious. Such a compound explicitly teaches away from a compound where the S group is attached directly at the 2 position of the compound.

US '542 does not overcome the deficiencies of US '240 as it provides nothing regarding the claimed compounds or possible modifications thereto. Moreover, no such allegations are made.

Withdrawal of this rejection is respectfully solicited.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Csaba Henter/

Csaba Henter, Reg. No. 50,908
Anthony J. Zelano, Reg. No. 27,969
Attorneys for Applicants

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1
2200 Clarendon Boulevard, Suite 1400
Arlington, VA 22201
Telephone: 703-243-6333
Facsimile: 703-243-6410
Attorney Docket No.:MERCK-3028

Date: August 20, 2008

K:\Merck\3000 - 3999\3028\Reply Aug 08.doc